United States Court of Appeals for the Federal Circuit

03-1327
(Serial No. 08/485,129)

IN RE DAVID WALLACH, HARTMUT ENGELMANN,
DAN ADERKA, DANIELA NOVICK, and MENACHEM RUBINSTEIN

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Appealed from: United States Patent and Trademark Office
Board of Patent Appeals and Interferences

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DECIDED: August 11, 2004

Before MAYER, Chief Judge, LOURIE and GAJARSA, Circuit Judges.

LOURIE, Circuit Judge.

David Wallach, Hartmut Engelmann, Dan Aderka, Daniela Novick, and Menachem Rubinstein (collectively, "Appellants") appeal from the decision of the United States Patent and Trademark Office ("PTO") Board of Patent Appeals and Interferences affirming the rejection of claims 11-13, 35-38, 43, 44, 46-49, 51-54, 56-61, 63, and 64 of United States patent application 08/485,129 under the written description requirement of 35 U.S.C. § 112. In re Wallach, Appeal No. 2002-1363 (Bd. Pat. Apps. & Interfs. Dec. 26, 2002). We affirm.

BACKGROUND

In the 1980s, Appellants apparently discovered two specific proteins isolated from human urine that, among other things, selectively inhibit the cytotoxic effect of tumor necrosis factor ("TNF"). They named the compounds TNF binding proteins I & II ("TBP-I" and "TBP-II"). After obtaining a partial amino acid sequence of the N-terminal portion of TBP-II and determining that the complete protein has a molecular weight of about 30 kilodaltons ("kDa") when measured by sodium dodecyl sulfate polyacrylamide gel electrophoresis ("SDS-PAGE") under reducing conditions, Appellants filed a patent

application including, inter alia, claims directed to proteins having that molecular weight and partial sequence (i.e., threonine-proline-tyrosine-alanine-proline-glutamic acid-proline-glycine-serine-threonine, or "Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr") and having the ability to inhibit the cytotoxic effect of TNF. Appellants' application also included claims to isolated DNA molecules that encode the claimed proteins. The PTO issued a restriction requirement and Appellants filed divisional applications. The claims directed to the proteins having the stated partial sequence are currently involved in an interference proceeding and are not at issue here. The claims at issue, those directed to the DNA, were rejected under § 112 "as based on a specification which does not provide an adequate written description of the claimed invention." Wallach, slip op. at 2. After several unsuccessful attempts to traverse that rejection, Appellants appealed to the Board.

Citing this court's decisions in Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed. Cir. 1991), Fiers v. Revel, 984 F.2d 1164 (Fed. Cir. 1993), and Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997), the Board affirmed the examiner's rejection. In particular, the Board held that "(1) applicants do not describe the genetic material sought to be patented in claim 11 with sufficient specificity in their specification; and (2) the examiner did not err in finding that claim 11 is based on a specification which does not provide adequate, written descriptive support for the claimed subject matter." Wallach, slip op. at 8-9.[1]

Appellants now appeal. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A).

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[1] The Board treated all of the appealed claims as standing or falling together with claim 11, pursuant to 37 C.F.R. § 1.192(c)(7), and decided the appeal on the basis of that claim alone. Wallach, slip op. at 5. Appellants do not challenge the Board on that point, and we likewise decide this appeal only on the basis of that claim.

DISCUSSION

Claim 11 of the '129 application reads as follows:

> 11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II, said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

On appeal, Appellants argue that the PTO has effectively conceded that the TBP-II protein, which the claimed isolated DNA encodes, is sufficiently described in the specification to comply with § 112, because the claims of United States patent application 07/930,443, of which the '129 application is a division (which, by definition, has the same specification), have been allowed but for their involvement in an interference proceeding. According to Appellants, those claims do not differ in substance from the present claims except insofar as they are directed to a partial protein sequence, rather than to the DNA sequences encoding the protein. Appellants contend that that is not a meaningful distinction, because the genetic code is based on an unequivocal correspondence between amino acids and encoding DNA codons, and determination of the amino acid sequence of a protein automatically puts one in possession of all DNA sequences encoding that protein. Appellants also argue that the complete amino acid sequence of a protein is an inherent property of an isolated protein that has been fully characterized by partial amino acid sequence and other characteristics, and that the complete amino acid

sequence of a protein therefore puts one in possession of all DNA sequences encoding it. Therefore, according to Appellants, the specification establishes that the present inventors were in fact in possession of the entire claimed genus of DNA sequences at the time the application was filed.

Appellants also argue that this case is distinguishable from past written description cases such as Amgen v. Chugai and Fiers, because Appellants have provided an actual amino acid sequence that is encoded by the claimed DNA, not simply the name of the protein and a statement that the DNA can be obtained by reverse transcription. Appellants contend that this case is also distinguishable from Lilly because the inventors here are not attempting to claim DNA molecules encoding a plurality of unknown proteins from various species having no common features, but only those encoding the single protein sequence that is actually set forth in the specification. Finally, Appellants argue that, because there is a known correlation between the function (i.e., encoding a specified amino acid sequence) and structure, this is the quintessential example of the sort of functional description permitted by § 112 in view of our decision in Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316 (Fed. Cir. 2002). Appellants argue that our recent decision in Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313 (Fed. Cir. 2003), which issued after the Board's opinion in the present case, reaffirmed that § 112 only requires a court to determine whether a specification conveys to one of ordinary skill in the art as of the filing date that the inventors invented the claimed subject matter.

The PTO responds by arguing that Appellants' specification includes neither any actual DNA sequence within the scope of the claims nor the complete amino acid sequence of the TBP-II protein, but only the sequence of ten out of the 185-192 amino

acids that make up the protein. Furthermore, the PTO argues, the only disclosed function of the claimed DNA molecules is to encode the TBP-II protein, and no information is provided from which the claimed DNA molecules can be distinguished from other DNA molecules. According to the PTO, the identity of the nucleic acid encoding a protein is not an inherent property of the protein. If Appellants' reasoning were accepted, the PTO asserts, the result would be that the disclosure of an isolated protein would be prior art under § 102 with respect to claims directed to any nucleic acid encoding the protein. Finally, the PTO contends, substantial evidence supports the Board's factual finding that Appellants' specification does not adequately describe the claimed genus of DNA molecules.

As a preliminary matter, we agree with Appellants that the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art at the time the '129 application was filed may have therefore been in possession of the entire genus of DNA sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious. Cf. In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995). Thus, for example, the RNA molecules required to encode the described amino acid sequence must necessarily have the following sequence: ACN-CCN-UAY-GCN-CCN-GAR-CCN-GGN-(UCN or AGY)-ACN, where N is A, G, C, or U; Y is U or C; and R is G or A. See James D. Watson et al., Molecular Biology of the Gene 356-57 (3d ed. 1977), cited in '129 application. A claim to the genus of DNA molecules complementary to the RNA having the sequences encompassed by that formula, even if defined only in terms of the protein sequence that

the DNA molecules encode, while containing a large number of species, is definite in scope and provides the public notice required of patent applicants. Indeed, the PTO's Manual of Patent Examining Procedure ("MPEP") states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 2 2001).

Moreover, we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that it is, as explained above, a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it.

Nonetheless, Appellants did not claim the nucleic acid molecules that encode the simple protein sequence that they disclosed. Rather, they claimed the nucleic acids encoding a protein for which they provided only a partial sequence. Appellants concede that it is now known that urinary TBP-II has a sequence of 185-192 amino acids. Without the approximately 95% of the amino acid sequence that Appellants did not disclose, we cannot say that the DNA molecules claimed in the '129 application have been described. As the MPEP explains, "disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention." MPEP § 2163.II.A.3.a.i. The Board's decision was thus consistent with its guidance in the

MPEP. Here, Appellants disclosed a partial structure and possibly sufficient additional characterization of the TBP-II protein to satisfy the PTO that they were in possession of the claimed subject matter in their '443 application, but that additional characterization contributes little, if anything, to the description of the DNA molecules claimed in the '129 application.

Appellants argue that "[a]s appellants have demonstrated possession of the TBP-II protein, appellants were also necessarily in possession of its inherent amino acid sequence, as well as all of the DNA sequences encoding that amino acid sequence." We disagree. Whether Appellants were in possession of the protein says nothing about whether they were in possession of the protein's amino acid sequence. Although Appellants correctly point out that a protein's amino acid sequence is an inherent property of the protein, the fact that Appellants may have isolated and thus physically possessed TBP-II does not amount to knowledge of that protein's sequence or possession of any of its other descriptive properties. Appellants have not provided any evidence that the full amino acid sequence of a protein can be deduced from a partial sequence and the limited additional physical characteristics that they have identified. Without that full sequence, we cannot agree with Appellants that they were possession of the claimed nucleic acid sequences. In Amgen v. Chugai, we explained that:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, . . . because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

927 F.2d at 1206. Until Appellants obtained the complete amino acid sequence of TBP-II, they had no more than a wish to know the identity of the DNA encoding it.

As Appellants point out, we have recognized that the written description requirement can in some cases be satisfied by functional description. See, e.g., Enzo, 296 F.3d at 1324 ("It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement."). Nonetheless, such functional description can be sufficient only if there is also a structure-function relationship known to those of ordinary skill in the art. As we explained above, such a well-known relationship exists between a nucleic acid molecule's structure and its function in encoding a particular amino acid sequence: Given the amino acid sequence, one can determine the chemical structure of all nucleic acid molecules that can serve the function of encoding that sequence. Without that sequence, however, or with only a partial sequence, those structures cannot be determined and the written description requirement is consequently not met. As we explained in Enzo, the Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) ("Guidelines"), state that

> the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. at 1106 (emphasis added).

Enzo, 296 F.3d at 1324-25 (emphasis added). Appellants have provided no evidence that there is any known or disclosed correlation between the combination of a partial structure of a protein, the protein's biological activity, and the protein's molecular weight, on the one hand, and the structure of the DNA encoding the protein on the other.

CONCLUSION

The Board correctly affirmed the examiner's determination that the specification of the '129 application does not provide an adequate written description of the pending claims. Accordingly, the Board's decision is

AFFIRMED.